REMARKS

Amendments to the Specification

The specification has been amended to provide the complete address of the hybridoma depository found on page 10, line 20 through page 11, line 7. *No new matter has been added.*

Claim Amendments

Claims 1-20 were pending. Claims 1-3, 10 and 15-16 have been amended as follows:

Claims 1-3 and 15-17 have been amended to specify that the agent is an "antibody or binding fragment thereof." Support for this amendment can be found throughout the present specification, for example, at page 3, lines 20-24; page 7, lines 22-28; and page 8, line 36 through page 9, line 17 of the specification as originally filed.

Claim 3 has been further amended to depend from claim 1 or claim 2 and to specify that the antibody binds to an Fc receptor at a site which not blocked by the natural ligand. Support for this amendment can be found throughout the present specification, for example, at page 3, lines 20-24; page 7, lines 22-28; and page 8, line 36 through page 9, line 17 of the specification as originally filed.

Claim 10 has been amended to specify the ATCC accession numbers for mab 22 and mab 32. Support for this amendment can be found within the present specification, for example, at page 10, line 35 through page 11, line 7 of the specification as originally filed.

New claim 21 further specifies that the compound comprises a photosensitizing moiety. Support for new claim 21 can be found throughout the present specification, for example, at page 5, lines 10-13, of the specification as originally filed.

The foregoing claim amendments should in no way be construed as an acquiescence to any of the Examiner's rejections and were made solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s). *No new matter has been added.*

Rejection of Claims 1 and 3-20 Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 3-20 are rejected as not being enabled because, according to the Examiner, "the specification, while being enabling for a first agent that does not bind in an Fc dependent manner to an Fc receptor on a macrophage, does not reasonably provide enablement for the full scope of 'a first agent which binds to an Fc receptor at a site which is distinct from that bound by endogenous immunoglobulins.'" Moreover, the Examiner cites Tzartos et *al.* in support of the proposition that "it would be outside the realm of routine experimentation" and "impossible to identify all the sites that are potentially bound by endogenous immunoglobulin."

First, based on the foregoing claim amendments, Applicant notes that this rejection is moot as it pertains to claims 1 and 4-20. With respect to claim 3, Applicant respectfully traverses this rejection. However, to expedite prosecution and allowance of the pending claims, claims 1 and 3 have been amended to specify that the first agent within the claimed compound is "an antibody or binding fragment thereof" which binds to an Fc receptor at a site which is "not blocked by the natural ligand", *i.e.*, binds to an Fc receptor outside of the natural ligand binding site.

Indeed, Applicant respectfully notes that the generation of antibodies that bind to Fc receptors without being blocked by the natural ligand were fully enabled at the time of filing, as evidenced by, for example, by U.S. Patent No. 4,954,617 (explicitly incorporated by reference in the present application at page 10, lines 29-31). This patent teaches routine methods for generating and identifying antibodies that bind to Fc receptors without being blocked by the natural ligand. As such, this subject matter is presumed enabled by the specification of the '617 patent. Moreover, since issuance of the '617 patent, the skill in the art has further developed for generating such antibodies.

Based on the foregoing, Applicant respectfully requests that the Examiner reconsider and withdraw the foregoing rejection under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 10 and 11 Under 35 U.S.C. § 112, First Paragraph

Claims 10 and 11 are rejected as failing to comply with the enablement requirement. Specifically, the Examiner indicates that the enablement requirement may be satisfied by a deposit of the cell lines recited in claims 10 and 11, *i.e.*, mab 22, 32, 197 and H22. Additionally, the Examiner notes "that the antibodies have been deposited with the ATCC (paragraph bridging

pages 10-11 of the specification), however, the terms of the deposit are not disclosed and the address of the depository is not included."

Applicant respectfully disagrees. Mab 22, 32 and H22 have indeed been deposited. However, to expedite prosecution and allowance of the pending claims, and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended claim 10 to delete reference to mab 197, thereby rendering this rejection moot with respect to mab 197.

With respect to the remaining cell lines recited in claim 10, Applicant submits herewith copies of the deposit receipts pertaining to mab 22, 32 and H22 (Appendices A-C, respectively). As indicated on the enclosed receipts, mab 22 was deposited on July 9, 1996, mab 32 was deposited on July 1, 1987, and H22 was deposited on November 4, 1992, with the ATCC located at P.O. Box 1549, Manassas, VA 20108 USA. The relevant portion of the specification has also been amended to provide this information. These deposits were made under the terms of the Budapest Treaty and comply with 37 C.F.R. § 1.808. In addition, Applicants state herein that the deposits will irrevocably and without restriction or condition be released to the public upon issuance of a patent based on the above-identified patent application.

Based on the foregoing, Applicant respectfully submits that claims 10 and 11 are fully enabled and requests that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 1-20 Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1-20 under 35 U.S.C. § 112, second paragraph, as being indefinite based on the phrase "a first agent which binds to an Fc receptor at a site which is distinct from that bound by endogenous immunoglobulins."

Applicant respectfully disagrees. However, to expedite prosecution and allowance of the pending claims, and in no way acquiescing to the validity of the Examiner's rejection, claim 3 has been amended to specify that the first agent is an antibody (or binding fragment thereof) which binds to an Fc receptor at a site which is "not blocked by the natural ligand," thereby obviating this rejection.

Claim 10 is also rejected because, according to the Examiner, "mab 22, 32 and 197" should be defined by a corresponding accession or deposit number from an acceptable depository. Applicant respectfully disagrees. However, to expedite prosecution and allowance of the pending claims, as discussed above, claim 10 has been amended to include the relevant ATCC accession numbers for mabs 22 and 32 and to delete reference to mab 197.

Based on the foregoing, Applicant requests reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 1-20, 12-13 and 15-20 Under 35 U.S.C. § 103(a)

Claims 1-20, 12-13 and 15-20 are rejected as being unpatentable over Fanger *et al.* (U.S. Patent No.: 5,635,600) in view of Deo *et al.* (U.S. Patent No. 5,922,845). The Examiner relies on Fanger *et al.* as teaching the use of a compound comprising a first agent that is an anti-FcγR antibody (such as a monoclonal antibody selected from the group consisting of mAbs 22, 32 and 197) and a second agent that is a toxin (such as ricin) or a liposome containing anticancer drugs to kill macrophages in some hematological cancers. The Examiner further relies on Fanger *et al.* as teaching that the anti-FcγR antibodies do not interfere with the binding of IgG to the Fc receptor.

While the Examiner acknowledges that Fanger *et al.* do not teach topical, subcutaneous or intradermal administration or a first agent that is directed to Fcα receptors, the Examiner alleges that Deo *et al.* cures this deficiency. Specifically, the Examiner relies on Deo *et al.* as teaching antibodies (such as a single chain antibody) that bind to Fc receptors on macrophages, can be administered subcutaneously or intradermally, and do not interfere with Fc-mediated binding of endogenous IgA. Applicant respectfully traverses this rejection.

The claimed invention is drawn to methods for selectively reducing the number or activity of macrophages within a localized area of tissue by topically, intradermally or subcutaneously administering an anti-FcR antibody (or binding fragment thereof) and an agent which kills or reduces the activity of the macrophages, *e.g.*, a toxin. While the primary reference, Fanger *et al.*, describe the anti-FcγR antibody-containing compositions encompassed by the pending claims, Fanger *et al.* fail to teach or suggest using such compositions for "selectively reducing the number or activity of macrophages within a localized area of tissue" or "treating a disease in a subject characterized by aberrant activity or numbers of macrophages within a selected area of the subject," as claimed.

Indeed, Fanger *et al.* teach away from the claimed methods by describing methods for reducing Fc receptors expressed by monocytes (*e.g.*, in the treatment of rheumatoid arthritis), using anti-FcR antibodies alone and not in conjunction with an agent which kills or reduces the activity of the macrophages, *e.g.*, a toxin, as currently claimed. Specifically, the Examiner refers

to the passage at column 7, lines 32-40, which describes the treatment of autoimmune disease and states that:

> The anti-FcR antibody of this invention can be employed to modulate Fc receptor levels on monocytic cells. For example, in auto-immune diseases (such as rheumatoid arthritis) the antibody can be administered in a form that induces "capping" and elimination of Fc receptors on the cell surface. The reduction of Fc receptors can interfere with monocyte clearance of antibody coated self-cells in patients. Mixtures of anti-Fc receptor antibodies can also be used for this purpose.

However, this passage relates to use of the "plain" unconjugated antibody alone (rather than together with a second agent as specified by the present claims) because if the antibody were conjugated to a second active agent (*e.g.*, a toxin such as ricin, as claimed), it would just kill the cell rather than influencing FcR "capping" as taught in the foregoing passage by Fanger *et al.*

Moreover, the only description regarding the use of an anti-FcR immunotoxin (*i.e.*, anti-FcR antibody linked to a toxin, as encompassed by the claims) pertains to killing FcR-expressing cells, such as cancer cells, *e.g.*, myeloid leukemia cells (see, col.7, lines 3-31) and not macrophages, as claimed. Accordingly, one of ordinary skill in the art, at the time of filing the present application, would not have been motivated, nor have had a reasonable expectation of success, at arriving at the claimed methods of treatment based on the teachings of Fanger *et al.*

The secondary reference, Deo *et al.*, does not make up for the aforementioned deficiencies of Fanger *et al.* Deo *et al.* teach the use of antibodies to *enhance* the function of macrophages and fail to describe any methods for reducing the number or activity of such cells. Therefore, there would have been no motivation whatsoever to have combined the teachings of Deo *et al.* with Fanger *et al.* Even if one would have combined these references, which Applicant does not concede would have occurred, such a combination would still fail to teach or suggest the claimed methods.

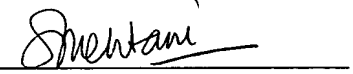
Accordingly, based at least on the foregoing, the cited references, either alone or in combination, fail to teach or suggest the claimed methods. Therefore, the claimed methods are patentable.

CONCLUSION

In view of the above amendments and remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicant's Attorney could be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: January 2, 2007

Respectfully submitted,

By 

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12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)881-2600 Telex: 898-055 ATCCNORTH

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10

To: (Name and Address of Depositor or Attorney)

Michael W. Fanger
Department of Microbiology
Dartmouth Medical School
Hanover, New Hampshire 03756

Deposited on Behalf of: Michael W. Fanger

Identification Reference by Depositor	ATCC Designation
Hybridoma cell, 32.2	HB 9469

The deposit was accompanied by: ___ a scientific description ___ a proposed taxonomic description indicated above.

The deposit was received July 1, 1987 by this International Depository Authority and has been accepted.

AT YOUR REQUEST:

X We will inform you of requests for the strain for 30 years.
___ We will not inform you of requests for the strain.
___ The strain is available to the scientific public upon request as of

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with a living culture of the same.

The strain will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested July 10, 1987. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Rockville, MD 20852 USA

Signature of person having authority to represent ATCC: Bobbie A. Brandon
(Mrs.) Bobbie A. Brandon, Head, Patent Depository

Date: July 10, 1987

cc: Giulio DeConti, Esq.

Form BP 4/9

American Type Culture Collection

12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 898-055 ATCCNORTH • FAX: 301-770-2587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Medarex, Inc.
Attention: Nathan B. Dinces, Ph.D.
12 Commerce Avenue
West Lebanon, NH 03784

Deposited on Behalf of: Medarex, Inc.

Identification Reference by Depositor:	**ATCC Designation**
Humanized 22 NSO cell line (mouse myeloma cell line O22HU-NSO secreting genetically engineering antibody 022 HU), HA022CL1	CRL 11177

The deposit was accompanied by: __ a scientific description __ a proposed taxonomic description indicated above.

The deposit was received November 4, 1992 by this International Depository Authority and has been accepted.

AT YOUR REQUEST:

X We will not inform you of requests for the strain.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested November 11, 1992. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Bobbie A. Brandon

Date: November 12, 1992

Bobbie A. Brandon, Head, ATCC Patent Depository

cc: Giulio DeConti

Form BP4/9

Appendix C

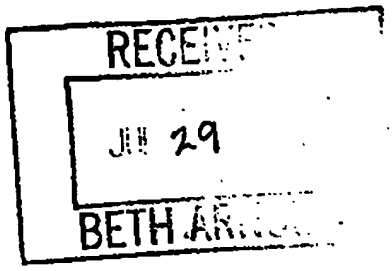
American Type Culture Collection

12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 908-768 ATCCROVE • FAX: 301-816-4366

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2



To: (Name and Address of Depositor or Attorney)

Medarex, Inc.
Attn: Michael Appelbaum
1545 Rt. 22 East
Annandale, NJ 08801

Deposited on Behalf of: Medarex, Inc.

Identification Reference by Depositor:	**ATCC Designation**
Hybridoma murine cell mAb 22	HB-12147

The deposit was accompanied by: ___ a scientific description _ a proposed taxonomic description indicated above.

The deposit was received July 9, 1996 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested July 24, 1996. On that date, the culture was viable.

Intemational Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Barbara M. Hailey

Barbara M. Hailey, Administrator, Patent Depository

Date: July 24, 1996

cc: Beth Arnold, Esq. (Ref. No. MXI-031CN3)